

Serial No: 08/870,199
Filed: June 5, 1997
Docket: 1650B US

*Last
amend*

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

amended
Claim 1 (original) An improved composition for physiological applications, said composition containing hydroxypropylmethylcellulose in a physiological salt solution, the improvement comprising a hydroxypropylmethylcellulose solution free of harmful particulate matter and gels greater than 0.5 μm in diameter, said viscoelastic solution having a zero shear viscosity in excess of 15,000 cps, an average molecular weight in excess of 250,000 Daltons and being pyrogen free and non-toxic when a therapeutically effective amount of said solution is injected into a human body.

Claim 2 (original) The improved composition of claim 1 wherein said composition being pyrogen free and non-toxic when a therapeutically effective amount of the solution is injected into a human eye.

Claim 3 (original) The viscoelastic solution of claim 2 wherein the hydroxypropylmethylcellulose is present in a concentration from about 2.0% to about 2.5%.

Claim 4 (original) The viscoelastic solution of claim 2 wherein the viscosity of the solution is from about 25,000 centipoise to about 40,000 centipoise.

Claim 5 (original) The viscoelastic solution of claim 2 wherein the average molecular weight of the hydroxypropylmethylcellulose is greater than about 375,000 but less than 420,000.

Claim 6 (original) The viscoelastic solution of claim 2 prepared from a blend of a first hydroxypropylmethylcellulose having a first molecular weight and a

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second hydroxypropylmethylcellulose having a greater molecular weight, the blend being processed to produce the particulate free, pyrogen free, and non-toxic solution.

Claim 7 (original) The viscoelastic solution of claim 6 wherein the blend is processed by filtration, redissolving and removal of low molecular weight material, mid-process autoclaving and removal of dissolved gases.

Claim 8 (original) The viscoelastic solution of claim 7 wherein the hydroxypropylmethylcellulose in the viscoelastic solution after processing has an average molecular weight greater than the average molecular weight of the first hydroxypropylmethylcellulose or the second hydroxypropylmethylcellulose.

Claim 9 (original) The viscoelastic solution of claim 6 wherein the first hydroxypropylmethylcellulose has an average molecular weight of about 85,000 and the second hydroxypropylmethylcellulose has an average molecular weight of about 220,000.

Claim 10 (original) The viscoelastic solution of claim 8 wherein the average molecular weight of the hydroxypropylmethylcellulose after processing is greater than 375,000 but less than 420,000.

Claim 11 (original) The viscoelastic solution of claim 6 having a hydroxypropylmethylcellulose concentration of about 2.3%.

Claim 12 (original) The viscoelastic solution of claim 5 wherein the hydroxypropylmethylcellulose has an average molecular weight of about 410,000.

Claim 13 ^{*amended*} (original) A process for preparing a viscoelastic solution of hydroxypropylmethylcellulose in a physiological salt solution, the composition having a zero shear viscosity in excess of 15,000 cps and being free of harmful particulate material and gels greater than 0.5 μ m in diameter and being pyrogen free

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and non-toxic when a therapeutically effective amount of said solution is injected into a human eye, the process comprising the steps of:

- a) dispersing the hydroxypropylmethylcellulose in the salt solution to form a suspension,
- b) heating the suspension of step (a) to about 95°C., allowing any undissolved material to settle and discarding the supernatant liquid above the undissolved material,
- c) resuspending the undissolved material to form a second suspension of hydroxypropylmethylcellulose and heating the second suspension to form a thick gel,
- d) filtering the gel through a series of filters to form a clean solution,
- e) autoclaving the clean solution,
- f) cooling the autoclaved clean solution and filtering the cooled solution, and
- g) degassing the filtered cooled solution.

[the series including a final filter having 0.5 μ m openings]

Claim 14 (original) The process of claim 13 wherein the physiological salt solution has a pH of about 8.7 and contains NaCl, KCl, $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{MgCl} \cdot 6\text{H}_2\text{O}$, $\text{NaC}_2\text{H}_3\text{O}_2 \cdot 3\text{H}_2\text{O}$, $\text{Na}_3\text{C}_6\text{HO}_7 \cdot 2\text{H}_2\text{O}$.

Claim 15 (original) The process of claim 13 wherein the hydroxypropylmethylcellulose dispersed in the aqueous salt solution is a blend of a first hydroxypropylmethylcellulose having a first molecular weight and a second hydroxypropylmethylcellulose having a higher molecular weight.

Claim 16 (original) The process of claim 15 wherein the first hydroxypropylmethylcellulose has a molecular weight of about 85,000 Daltons and the second hydroxypropylmethylcellulose has a molecular weight of about 220,000 Daltons.

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Claim 17 (original) The process of claim 15 wherein the weight of the first hydroxypropylmethylcellulose in the suspension is about the weight of the second hydroxypropylmethylcellulose.

Claim 18 (original) The process of claim 15 wherein the hydroxypropylmethylcellulose in the suspension is about 3% by weight.

Claim 19 (original) The process of claim 13 wherein the concentration of the hydroxypropylmethylcellulose in the degassed solution is from about 2.0% to about 2.5%.

Claim 20 (original) The process of claim 13 wherein the concentration of the hydroxypropylmethylcellulose in the degassed solution is about 2.3%.

Claim 21 (original) The process of claim 13 wherein the viscosity of the degassed solution is from about 25,000 centipoise to about 40,000 centipoise.

Claim 22 (original) The process of claim 13 wherein the viscosity of the degassed solution is about 40,000 centipoise.

Claim 23 (original) The process of claim 13 wherein the molecular weight of the hydroxypropylmethylcellulose in the degassed solution is greater than about 375,000 but less than about 420,000.

Claim 24 (original) The process of claim 11 wherein the molecular weight of the hydroxypropylmethylcellulose in the degassed solution is about 410,000.

Claim 25 (original) A viscoelastic composition for injection into a human eye, the viscoelastic composition comprising hydroxypropylmethylcellulose in a physiological salt solution,

the hydroxypropylmethylcellulose having an average molecular weight

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greater than about 375,000 but less than about 420,000 and being present in a concentration from about 2.0% to about 2.5%,

the composition having a viscosity from about 25,000 centipoise to about 40,000 centipoise being free of harmful particulate matter and gels greater than 0.5 μm in diameter and being pyrogen free and nontoxic.

Claim 26 (original) The viscoelastic composition of claim 25 wherein the concentration of the hydroxypropylmethylcellulose is about 2.3%, the average molecular weight of the hydroxypropylmethylcellulose is about 409,800 and the zero shear viscosity of the composition is about 40,000 centipoise.

Claim 27 (new) A process of preparing a sterile solution of hydroxypropylmethylcellulose in an aqueous solution, the sterile solution having a zero shear viscosity in excess of 15,000 cps and being non-toxic, non-pyrogenic, and substantially free of particulate matter and gels greater than 0.5 μm in diameter and harmful to the human eye, the process comprising the steps of:

- a) dispersing hydroxypropylmethylcellulose in a first part of the aqueous solution to form a suspension;
- b) allowing the suspension to settle to yield a supernatant and a sediment comprising high molecular weight hydroxypropylmethylcellulose;
- c) discarding the supernatant, and leaving the sediment;
- d) resuspending the sediment in a second part of the aqueous solution to form a gel;
- e) filtering the gel through a plurality of successively finer filters to remove harmful particulate and gelatinous matter to form a clean solution; and
- f) sterilizing the clean solution.

Claim 28 (new) The process of step 27, wherein step a) is performed at a sufficiently elevated temperature to solvate low molecular weight

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hydroxypropylmethylcellulose, and step e) is performed at a sufficiently elevated temperature to significantly reduce the viscosity of the gel.

Claim 29 (new) The process of claim 28, wherein the sterilization of the clean solution is effected by autoclaving.

Claim 30 (new) The process of claim 29, comprising the further steps of:

- a) cooling the autoclaved clean solution;
- b) filtering the cooled solution; and
- c) degassing the filtered, cooled solution.

Claim 31 (new) An improved composition for physiological applications, said composition containing hydroxypropylmethylcellulose in a physiological salt solution, the improvement comprising a hydroxypropylmethylcellulose solution free of particulate matter and gels greater than 0.5 μ m in diameter, said viscoelastic solution having a zero shear viscosity in excess of 15,000 cps, an average molecular weight in excess of 250,000 Daltons and being pyrogen free and non-toxic when a therapeutically effective amount of said solution is injected into a human body.

Claim 32 (new) The improved composition of claim 31 wherein said composition being pyrogen free and non-toxic when a therapeutically effective amount of the solution is injected into a human eye.

Claim 33 (new) The viscoelastic solution of claim 32 wherein the hydroxypropylmethylcellulose is present in a concentration from about 2.0% to about 2.5%.

Claim 34 (new) The viscoelastic solution of claim 32 wherein the viscosity of the solution is from about 25,000 centipoise to about 40,000 centipoise.

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Claim 35 (new) The viscoelastic solution of claim 32 wherein the average molecular weight of the hydroxypropylmethylcellulose is greater than about 375,000 but less than 420,000.

Claim 36 (new) The viscoelastic solution of claim 32 prepared from a blend of a first hydroxypropylmethylcellulose having a first molecular weight and a second hydroxypropylmethylcellulose having a greater molecular weight, the blend being processed to produce the particulate free, pyrogen free, and non-toxic solution.

Claim 37 (new) The viscoelastic solution of claim 36 wherein the blend is processed by filtration, redissolving and removal of low molecular weight material, mid-process autoclaving and removal of dissolved gases.

Claim 38 (new) The viscoelastic solution of claim 37 wherein the hydroxypropylmethylcellulose in the viscoelastic solution after processing has an average molecular weight greater than the average molecular weight of the first hydroxypropylmethylcellulose or the second hydroxypropylmethylcellulose.

Claim 39 (new) The viscoelastic solution of claim 36 wherein the first hydroxypropylmethylcellulose has an average molecular weight of about 85,000 and the second hydroxypropylmethylcellulose has an average molecular weight of about 220,000.

Claim 40 (new) The viscoelastic solution of claim 38 wherein the average molecular weight of the hydroxypropylmethylcellulose after processing is greater than 375,000 but less than 420,000.

Claim 41 (new) The viscoelastic solution of claim 36 having a hydroxypropylmethylcellulose concentration of about 2.3%.

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Claim 42 (new) The viscoelastic solution of claim 35 wherein the hydroxypropylmethylcellulose has an average molecular weight of about 410,000.

Claim 43 (new) A process for preparing a viscoelastic solution of hydroxypropylmethylcellulose in a physiological salt solution, the composition being free of particulate material and gels greater than 0.5 μm in diameter and being pyrogen free and non-toxic when a therapeutically effective amount of said solution is injected into a human eye, the process comprising the steps of:

- a) dispersing the hydroxypropylmethylcellulose in the salt solution to form a suspension,
- b) heating the suspension of step (a) to about 95° C, allowing any undissolved material to settle and discarding the supernatant liquid above the undissolved material,
- c) resuspending the undissolved material to form a second suspension of hydroxypropylmethylcellulose and heating the second suspension to form a thick gel,
- d) filtering the gel through a series of filters, the series including a final filter having 0.5 μm openings to form a clean solution,
- e) autoclaving the clean solution,
- f) cooling the autoclaved clean solution and filtering the cooled solution,
and
- g) degassing the filtered cooled solution.

Claim 44 (new) The process of claim 43 wherein the physiological salt solution has a pH of about 8.7 and contains NaCl, KCl, $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{NaC}_2\text{H}_3\text{O}_2 \cdot 3\text{H}_2\text{O}$, $\text{Na}_3\text{C}_6\text{HO}_7 \cdot 2\text{H}_2\text{O}$.

Claim 45 (new) The process of claim 43 wherein the hydroxypropylmethylcellulose dispersed in the aqueous salt solution is a blend of a first hydroxypropylmethylcellulose having a first molecular weight and a second hydroxypropylmethylcellulose having a higher molecular weight.

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Claim 46 (new) The process of claim 45 wherein the first hydroxypropylmethylcellulose has a molecular weight of about 85,000 Daltons and the second hydroxypropylmethylcellulose has a molecular weight of about 220,000 Daltons.

Claim 47 (new) The process of claim 45 wherein the weight of the first hydroxypropylmethylcellulose in the suspension is about the weight of the second hydroxypropylmethylcellulose.

Claim 48 (new) The process of claim 45 wherein the hydroxypropylmethylcellulose in the suspension is about 3% by weight.

Claim 49 (new) The process of claim 43 wherein the concentration of the hydroxypropylmethylcellulose in the degassed solution is from about 2.0% to about 2.5%.

Claim 50 (new) The process of claim 43 wherein the concentration of the hydroxypropylmethylcellulose in the degassed solution is about 2.3%.

Claim 51 (new) The process of claim 43 wherein the viscosity of the degassed solution is from about 25,000 centipoise to about 40,000 centipoise.

Claim 52 (new) The process of claim 43 wherein the viscosity of the degassed solution is about 40,000 centipoise.

Claim 53 (new) The process of claim 43 wherein the molecular weight of the hydroxypropylmethylcellulose in the degassed solution is greater than about 375,000 but less than about 420,000.

Claim 54 (new) The process of claim 41 wherein the molecular weight of the hydroxypropylmethylcellulose in the degassed solution is about 410,000.

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Claim 55 (new) A viscoelastic composition for injection into a human eye, the viscoelastic composition comprising hydroxypropylmethylcellulose in a physiological salt solution,

the hydroxypropylmethylcellulose having an average molecular weight greater than about 375,000 but less than about 420,000 and being present in a concentration from about 2.0% to about 2.5%,

the composition having a viscosity from about 25,000 centipoise to about

40,000 centipoise, being free of particulate matter and gels greater than 0.5 μ m in diameter and being pyrogen free and nontoxic.

Claim 56 (new) The viscoelastic composition of claim 55 wherein the concentration of the hydroxypropylmethylcellulose is about 2.3%, the average molecular weight of the hydroxypropylmethylcellulose is about 409,800 and the zero shear viscosity of the composition is about 40,000 centipoise.

Claim 57-58 (cancelled)